Reviewer's report

Title: Transplantation of Endothelial Progenitor Cells in Treating Rats with IgA Nephropathy

Version: 2 Date: 12 December 2013

Reviewer: Hiroyuki Inoshita

Reviewer's report:

This manuscript is easy to follow and partially contains interesting findings, however, major revisions are still required.

Major Compulsory Revisions

1. I strongly doubt that this rat model is used as IgAN model. Is this model already established as human IgAN model? Probably, IgA deposition and glomerular damage in this model is occurred by liver dysfunction due to CCL4, as you know CCL4 is generally used for experimental liver cirrhosis. Interstitial nephritis and glomerular damage might be directly affected by CCL4 and/or LPS injection. If the authors still would like to use this model, they should state this model is likely to be “secondary” IgAN rather than just IgAN.

2. According to the comment in #1 above, the authors should change the title which is misleading for me. For example, “Transplantation of endothelial progenitor cells in treating rats manifesting secondary IgA nephropathy-like phenotype”. The authors also should revise their Introduction, Methods, and Discussion in terms of secondary IgAN.

3. The authors should show electron microscopic study for glomeruli from EPCs group at pre- and post transplantation. How about electron dense deposit in mesangial area which is frequently observed in human IgAN? How about podocytic foot process effacement and endothelial cell damage?

4. The authors claim that endothelial cell damage in the rat model was improved by transplantation of EPC. They should show grade of hematuria (using dip sticks, hemoglobin ELISA, or something like that) at pre-transplantation, 3, 7, and 14 days after transplantation because hematuria generally indicates endothelial cell damage in glomerulonephritis.

5. In Subjects and Methods, Animal section, the author must state adequate reference instead of reference No.8 (Lou T et al. Nephrology 2006) which does not describe how to make the rat-model.

Minor Essential Revisions

1. The authors would better to spell out any numbers beginning a sentence.

2. PAM and Masson's trichrome staining might be added for evaluation of glomerular capillary and interstitium of kidney, respectively.

3. I would like to know whether IgA in this rat model has aberrant glycosylation or
not because aberrant glycosylated IgA has been frequently found from serum in human IgAN. Mass spectrometry or lectin ELISA might be performed to investigate the glycosylation.

4. To examine natural course of the IgAN-rats without EPCs transplantation, I would like to know urine protein excretion, BUN, Scr, hematuria at Day 0, 1, 3, 7, 14 in just IgAN-rat model group, too.

5. The authors demonstrate HIF-1alpha expression was decreased in EPCs group. How about other oxidative stress marker such as DCFDA or 8-OHdG?

Discretionary Revisions
None

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.